REMARKS

Reconsideration and allowance are respectfully requested in light of this amendment and the following remarks. Applicants have amended the claims to expedite prosecution of the application. This amendment is not intended to acquiesce to the rejections raised by the Examiner and Applicants reserve the right to pursue broader claim subject matter in follow-on applications.

Claims 1-3, 5-8 and 10-17 were provisonally rejected under the judicially created doctrine of obviousness-type double patenting. Claims 1-3, 5-8, 10-12 and 14-17 were rejected under 35 USC 102(a) as being anticipated by Schindler et al. (WO00/02851). Claims 1-3, 5-8, 10-12 and 14-17 were rejected under 35 USC §112, second paragraph, as being indefinite. Claims 12, 14, 16 and 17 were rejected under 35 USC 112, first paragraph as not enabling cancer and other diseases, although enabling for inflammation. Claim 15 was rejected under35 USC 101because the claim was not supported by either a step/process asserted utility or a well established utility.

Examiner searched for compounds of Formula I' where

X is -CONH-

A is pyridyl

Y is $-NHCH_2-$ or $-NHSO_2-$

R^1 is H

R^2 is substituted phenyl

R^3 is substituted phenyl.

Claims 4 and 9 were withdrawn from further consideration. Applicants believe that Claim 4 was withdrawn in error as the scope of the claim includes elected subject matter.

Claims 1-3, 5-8 and 10-17 were provisonally rejected under the judicially created doctrine of obviousness-type double patenting. Although the Applicants do not agree with the rejection, the provisional nature of the rejection is noted and Applicants request that the issue be deferred until such time as allowable subject matter has been indicated in either application. Alternatively, it is respectfully requested that both applications issue on the same day.

Claims 1-3, 5-8, 10-12 and 14-17 were rejected under 35 USC 102(a) as being anticipated by Schindler et al. (WO00/02851). Applicants disagree that Claims 2-3, and 5-8 are anticipated by Schindler et al. as they do not claim sulfonamides as "Y" substituents. Applicants request reconsideration of the rejections in view of amended Claim 1.

Claims 1-3, 5-8, 10-12 and 14-17 were rejected under 35 USC §112, second paragraph, as being indefinite. Claims 1-3, 5-8 and 10 were rejected as the Examiner believes the term "pharmaceutically-acceptable derivatives" is indefinite. The term is defined in the specification on page 41, lines 13-18.

Applicants request reconsideration of this rejection as the term is not indefinite. Claims 12, 14 and 16-17 were rejected because of the term "effective amount". Applicants request reconsideration of the rejections in view of the amended Claims.

Claims 12, 14, 16 and 17 were rejected under 35 USC 112, first paragraph as not enabling cancer and other diseases, although enabling for inflammation. Applicants respectfully disagree. Patent Law requires that a specification disclosure, which contains a teaching of how to make and use the claimed invention in terms that correspond in scope to those used in describing and defining the subject matter, must be taken as in compliance with the enablement requirement under 35 U.S.C. §112, first paragraph, unless there is reason to doubt the objective truth of the statements relied on for enabling support (see MPEP § 2164.02-2164.05).

Applicants respectfully submit that one skilled in the art would understand from Applicants Specification how to make and use the claimed compounds (see Applicants' Specification pages 52-64, 67-105 and 119-222). While working examples are not per se required for enablement, Applicants demonstrated that 30+ compounds of varying structures had at least an IC_{50} of less than 50nM in vitro models (see Applicants' Specification pages 216-218).

Further, in addition to the compounds made and tested, there is ample support in the art for the credibility of Applicants' invention. Cancer is a group of diseases characterized by dysregulated cell growth control. Growth of cancer cells is dependent on the continued supply of oxygen and nutrients that is delivered to them by vascular networks. Unless neovascularization occurs, tumor growth is limited by the diffusion limit for oxygen and does not progress beyond 1 to 2 mm in size. (Carmeliet P. Mechanisms of angiogenesis and arteriogenesis. *Nature Med.* 2000;6:389-395) In experimental models of cancer, blocking angiogenesis prevents tumor growth and/or progression. (Scappaticci FA. Mechanisms and future directions for angiogenesis-based cancer therapies. *J Clin Onc.* 2002;20:3906-3927.) The importance of angiogenesis in human cancer is supported by numerous clinicopathologic correlations, which link the production of proangiogenic substances by the cancer cells or the density of microvasculature in tumors to patient prognosis. (See Leek RD. The prognostic role of angiogenesis in breast cancer. *Anticancer Res.* 2001;21:4325-4332. Mehta R, Kyshtoobayeva A, Kurosaki T, et al. Independent association of angiogenesis index with outcome in prostate cancer. *Clin Cancer Res.* 2001;7:81-88. Papamichael D. Prognostic role of angiogenesis in colorectal cancer. *Anticancer Res.* 2001;21:4349-4354.)

The ability of in vitro endothelial proliferation assays such as that described in the subject application, to support treatment of VEGF-related angiogenesis and cancer claims is understood to one skilled in the art. See, for example: D. Wand et al. Expression and endosytosis of VEGF and its receptors in human colonic vascular endothelial cells. *Am J Phys. Gast. Live Physiology,* 282, G1088-96, 2002. W. Auerbach and R.

Auerbach. Angiogenesis Inhibition: A review. *Pharmac. Ther.* 63. 265-311, (1994). R. Bagley, et al. Endothelial Precursor Cells as a Model of Tumor Endothelium: Characterization and Comparison with Mature Endothelial Cells. *Cancer Res.* 63, 5866-73, (2003). L. Hennequin et al. Design and Structure-Activity Relationship of a New Class of Potent VEGF Receptor Tyrosine Kinase Inhibitors. *J. Med. Chem.* 42, 5369-89 (1999). D. Wang et al. Homeostatic Moduloation of Cell Surface KDR and Flt1 Expression and Expression of the Vascular Endothelial Cell Growth Factor (VEGF) Receptor mRNAs by VEGF. *J. Biol. Chem.* 275, 15905-11, (2000). M. Stewart, et al. The angiogenic receptor KDR is widely distributed in human tissues and tumours and relocates intracellularly on phosphorylation. An immunohistochemical study. *Histopath.* 43, 33-39 (2003). Copies of these references are provided in an accompanying Supplemental Information Disclosure Statement.

Thus Applicants respectfully submit that one skilled in the art would understand from Applicants' Specification how to make and use the compounds of the invention and that Claims 1-42 meet the requirements of 35 U.S.C. §112, first paragraph. Therefore, Applicants respectfully request that the rejection of Claims 1-42 under 35 U.S.C. §112, first paragraph, be withdrawn.

It is therefore respectfully submitted that Claims 1-4, 6-8, 10-14 and 16-42 are now in condition for allowance. Accordingly, reconsideration and withdrawal of the outstanding rejections, and allowance of Claims 1-4, 6-8, 10-14 and 16-42 are respectfully solicited.

Respectfully submitted,

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